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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/089,501	04/22/2002	Hiroyuki Saito	053466-0325	9449

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FOLEY AND LARDNER LLP
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
HAMUD, FOZIA M	

ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/089,501	SAITO ET AL.	
	Examiner	Art Unit	
	FOZIA M. HAMUD	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 November 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45-49 and 51-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45-49 and 51-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/17/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1a. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 17 November 2009 has been entered.

Status of Application/Claims:

1b. The Examiner and Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Examiner Fozia Hamud, Group Art Unit 1647.

1c. Claims 1-44 and 50 have been canceled. Claims 57-59 are added. Claims 45-49 and 51-59 are pending and under consideration.

Priority:

2. This application, filed 4/22/2002 claims priority to PCT/JPO0/06802, filed 9/29/2000, therefore the instant invention has been granted a priority date of 9/29/2000. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement:

3. The information disclosure statement filed on 17 November 2009 has been received and complies with the provisions of 37 CFR §1.97 and §1.98. It has been placed in the application file and the information referred to therein has been considered as to the merits.

Specification:

4. The abstract of the disclosure is objected to because (1) it is not limited to a single paragraph on a separate sheet within the range of 50 to 150 words and (2) it uses legal phraseology often used in patent claims, such as "means" and "said"

Correction is required. See MPEP § 608.01(b).

Claim Rejections - 35 USC § 102:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 45-49, 52, 53 and 55 are rejected under 35 U.S.C. 102(e) as being anticipated by Wong et al (U.S. Patent 5,986,065, EFD 3/10/1997). This rejection is maintained for reasons made of record in the previous Office Actions dated 4/4/2008, 12/23/2008, 06/04/2009 and for reasons set forth below.

Claims 45-49, 52, 53 and 55 are drawn to a method for suppressing hypertrophy of the vascular intima caused by expression of tissue factor in a patient in need thereof,

comprising administering to the patient a therapeutically effective amount of an antibody that binds to an inhibitory site for binding a complex of human tissue factor (human TF) and Factor VIIa to Factor X, upon binding to human TF, wherein the antibody is a humanized antibody or a chimeric antibody having a human antibody constant region, wherein the antibody is monoclonal, polyclonal, recombinant, altered or modified.

Wong et al disclose teach TF-specific antibodies that bind human TF and that inhibit the activation of Factor X by the TF/Factor VIIa complex, and can be used for treatment of, for example, restenosis. (See the abstract, Figs. 4, 6A, 6B, 7, column 3, lines 18-37, column 5, 19-35). The antibodies may be chimeric, or humanized, by using a human constant region with a non-human variable region (column 8, lines 46-67). The antibodies may be monoclonal or polyclonal and are modified, (see column 7, lines 46-49). The antibodies taught by Wong et al are used to prevent or inhibit restenosis or other thromboses following an invasive medical procedure such as arterial or cardiac surgery, e.g., angioplasty, (see column 3, lines 17-22).

Response to Arguments:

Applicants submit that the office is relying on inherency, however, no such inherency exists and that the Office's allegation is based on the antibodies of Wong and the presently claimed invention. Applicants argue that claims 45 are 53 are explicitly directed to methods of suppressing hypertrophy specifically for a patient in need thereof. Applicants further argue that the Office's reliance on the antibodies of Wong to reject the presently claimed invention, particularly when the presently claimed methods are directed to a specific treatment, is erroneous. Applicants submit that the Examiner's

assertion that the patient group 'in need thereof' to be treated by the instant claims and by Wong et al. would appear to be the same", is erroneous. Applicants argue that it matters little what the antibody of Wong is, because the present claims are directed to specific type of treatment methods for a specific type of a patient, the present claims should be interpreted accordingly.

This argument has been fully considered but is not deemed persuasive. It is acknowledged that instant claims are drawn to a method of treatment using antibodies and are not drawn to antibodies, however, Wong et al teaches antibodies. Wong also teaches using said antibodies in treating the same patient population as recited in the instant claims. Wong disclose that the invention provides methods for reducing tissue factor (TF) levels (column 3, lines 10-11). Wong also state that antibodies of the invention will be useful to modulate virtually any biological response mediated by FX binding to TF or the TF:VIIa complex, including blood coagulation, inflammation and other disorders (column 3, lines 12-16).

Applicants submit that the Office incorrectly interprets the present claims to encompass more than suppressing hypertrophy for a patient in need thereof, as specifically recited in the present claims. Applicants argue that the present claims are intended to recite a method of suppressing hypertrophy of the vascular intima for a patient in need thereof, and thus they should analogously be interpreted to suppress "hypertrophy of the vascular intima," per se, and not merely "symptoms associated" therewith. Applicants submit that Wong discloses only the prevention of thrombosis and blood clotting and does not at all teach the presently claimed methods of suppressing

"hypertrophy of the vascular intima caused by tissue expression" in a patient "in need thereof," as recited in independent claims 45 and 53. Applicants argue that hypertrophy of vascular intima is not thrombosis. The thrombosis prevention of Wong's teaching is distinct from the presently claimed hypertrophy suppression. Despite the fact that Wong mentions the term "restenosis," Wong's teaching in its entirety is related only to anticoagulant activity and has little to do with suppressing hypertrophy. Applicants submit that the Office also extrapolates and then alleges that the presently claimed hypertrophy "would encompass both early and late stages of restenosis". Applicants submit that the Office's reliance on a general descriptive term "restenosis" to produce its own definition for Wong's teaching and the presently claimed invention is unreasonable, especially when the Office's definition is contradictory to commonly understood knowledge. The Office asserts that because the present Specification does not provide a specific definition of the term "restenosis," the Office provides its own definition. Applicants respectfully submit that the term "restenosis" is known in the art and respectfully remind the Office that a patent need not teach, and preferably omits, what is well known in the art See, e.g., Hybritech, Inc. v. MonoclonalAntibodies, Inc., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986). In the September 3, 2009 reply, the Applicants submitted a specific reference to a chapter in Fuster et al. to demonstrate that the term restenosis is a general term that involves a series of distinct events, whereas Wong's teaching relates only to one stage that is distinct from what is presently claimed.

These arguments are considered, but are not deemed persuasive. The instant

claims are drawn to a method of suppressing "hypertrophy of the vascular intima", however, the instant specification does not define "hypertrophy of the vascular intima". Therefore, based upon the definitions of "hypertrophy" and "vascular intima" known in the art (see Stedman's Medical Dictionary 27th Edition), the Examiner has interpreted this phrase as meaning that the expression of tissue factor causes irregular formations or thickening of blood vessels. Restenosis is the development of a neointima (thickened layer or vessel) after angioplasty (see Fuster et al., page 148, column 2). Since the specification provides little guidance as to a clear definition of "hypertrophy of the vascular intima", the Examiner also looked to the specification for examples of possible patient populations that may experience hypertrophy of the vascular intima. Example 6 in the instant specification teaches that humanized anti-human TF antibody "i-b2" suppressed the hypertrophy of the intima (page 41, lines 5-7). The specification teaches that this indicates the "i-b2" antibody prevents the narrowing of the area of the lumen during the remote period by suppressing the growth of the blood vessel tissue itself, suggesting that it can prevent restenosis (page 41, lines 8-12). The animal model used in Example 6 of the specification is angioplasty in Cynomolgus monkeys (page 40). Wong et al. teach that the antibodies of the invention can be used to modulate virtually any biological response mediated by FX binding to TF or the TF:VIIa complex, including blood coagulation, inflammation and other disorders. Wong disclose the antibodies can be administered for invasive medical procedures, including angioplasty (column 3, lines 17-25). Hence, it is clear that the patient populations of the instant claims and of Wong et al. overlap. Wong et al. disclose administering the same tissue

factor antibodies to the same subject population as required by the instant claims. Therefore, suppression of hypertrophy of the vascular intima must have been inherently occurring in the prior art of Wong et al., absent evidence to the contrary (see *Ex parte Novitski*, 26 USPQ2d 1389 (BPAI 1993) ; see also *Integra LifeSciences I Ltd. V. Merck KGaA*, (DC SCalif) 50 USPQ2d 1846; *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977)). Furthermore, inherent anticipation does not require that one of ordinary skill in the art recognize an inherent feature in a prior art disclosure (*Schering Corp. v. Geneva Pharmaceuticals Inc.*, 67 USPQ2d 1664 (CAFC 2003); *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004)).

In the instant case, the specification does not teach how the encompassed patient population differs from the patient population of Wong et al. Neither does it teach that the anti-TF antibodies of the instant invention display properties other than anti-coagulant properties.

Applicants submit that the Office's analogy between an "argument of counsel" and a specific reference to "factual evidence" is unreasonable. However, to facilitate the Office's review, the Applicants submit herewith Exhibit A, which contains a copy of the aforementioned chapter; the section referenced in the previous reply is also explicitly marked. The Applicants also submit herewith an Ann Thorac Surg article by Thatte et al. as Exhibit B to provide additional support and respectfully direct the Office's attention to Fig. 1 and the description associated therewith in Exhibit B. Exhibits A and B together demonstrate that while each of the different events during restenosis might occasionally be mistakenly labeled as "restenosis," restenosis is understood by one of ordinary skill

in the art to involve a series of distinct events. Thus, although Wong might have mentioned the term "restenosis," Wong's teaching in its entirety is directed to anti-coagulant activity to prevent thrombosis and has little to do with suppressing the hypertrophy that occurs after thrombosis. The Office repeatedly directs the Applicants to col. 3, lines 18-37 of Wong, which as a matter of fact supports the Applicants' position. Col. 3, lines 18-37 of Wong reads "...alleviate various thromboses, particularly to prevent or inhibit restenosis, or other thromboses following an invasive medical procedure..." Both the plain language of this statement and ejusdem generis suggest that "restenosis" in the clause "particularly..." should be read together with and to refer to the "thromboses" in the phrase "various thromboses" immediately before and the phrase "other thromboses" immediately after. In fact, Wong does not contain the term "hypertrophy" at all in its disclosure. Accordingly, the Office has misconstrued Wong's teaching. Furthermore, in view of the foregoing, the Office's extrapolation from "hypertrophy of the intima," as recited in the present claims, to "thrombosis prevention" of Wong based solely on the fact that the general term "restenosis" is mentioned in Wong and Example 6 of the present Specification (see item (2), Advisory Action) is arbitrary and without basis.

These arguments are not found persuasive. It is acknowledged that the Wong et al reference does not contain the word “hypertrophy”. However, restenosis is defined by the submitted reference as the development of neointima that occurs following angioplasty, often leading to reclusion of the initial lesion. Wong et al clearly teach treating restenosis with anti-TF antibodies for reasons made of record. Thus, that is all

that is required to anticipate the instant claims, as restenosis is a prime example of "hypertrophy of the vascular intima", a term also not defined in the specification. "Hypertrophy" is, loosely, a growth of non-tumorous nature and "intima" is considered to be the innermost membrane of a vein, vessel, etc. Accordingly, since the antibodies of Wong et al have the same activity as those instantly claimed, they inherently have the same effect upon restenosis as the claimed antibodies.

Applicants argue that the Office appears to suggest that the Applicants have admitted that hypertrophy of vascular intima is restenosis.

This argument is considered, and it is acknowledged that Applicants consistently argue that hypertrophy of vascular intima is not the same as restenosis. However, it is noted that the only working example of the claimed methods in the specification would appear to treat restenosis due to the temporal aspect of administration of the claimed antibodies before vascular injury, (see the sentence bridging pages 40 and 41). Thus, the patient group "in need thereof" to be treated by the instant claims and by Wong et al would appear to be the same.

Allowable Subject Matter

6. Claims 51, 54 and 56 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

7. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

7a. SATO, et al (U.S. Patent No. 6,677,436), an antibody that comprises the heavy and light chains recited in claims 51, 54, 55 and 56, (see SEQ ID NOs: 166, 173, 180 and 183 of the Sato et al reference, which correspond to SEQ ID NOs: 29, 88, 59 and 98, respectively).

7b. Lowe et al, (U.S. Patent No. 6,703,494),which teaches anti-tissue factor antibodies.

Conclusion:

8. No claim is allowed.

Advisory Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to FOZIA M. HAMUD whose telephone number is (571)272-0884. The examiner can normally be reached on Monday-Friday: 8:00 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Fozia Hamud
Patent Examiner
Art Unit 1647
11 January 2010

/Bridget E Bunner/
Primary Examiner, Art Unit 1647